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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

ILLUMINA, INC. and ILLUMINA CAMBRIDGE LTD., Plaintiffs, v. COMPLETE GENOMICS, INC., Defendant.	Case No. 3:12-cv-01465-BEN-BGS **ILLUMINA'S OPENING CLAIM CONSTRUCTION BRIEF** Hon. Roger T. Benitez Date: July 11, 2013 Time: 9:00 A.M. Room: 4B

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I. Introduction

The patent-in-suit, U.S. Patent No. 8,192,930 ("the '930 patent"), describes and claims specific methods for obtaining sequence information from nucleic acids such as DNA. These "paired-end" sequencing methods enable one to successfully "read" sequence information sequentially from two distinct, separate regions on a single piece of DNA.

Plaintiff Illumina, Inc. (and its subsidiary, Illumina Cambridge Ltd.) (collectively, "Illumina") is one of the leading companies in genetic analysis. The '930 patent resulted from Illumina's pioneering work in next-generation DNA sequencing technologies. Illumina employs its patented paired-end reading method in its highly successful commercial sequencing instruments, which enable scientists to sequence an entire human genome in just over a day.

Defendant Complete Genomics, Inc. ("CGI"), a wholly-owned subsidiary of BGI-Shenzhen, is a recent entrant to the field of genetic analysis. Illumina asserts that CGI infringes claim 1 of the '930 patent by using what CGI calls its Combinatorial Probe Anchor-Ligation ("cPAL") technology.

The parties disagree about the construction of five terms in claim 1. Illumina's proposed constructions are drawn from the language used in claim 1 and the specification of the '930 patent, and will aid the jury in understanding the meaning of the claim. In contrast, in an effort to create non-infringement defenses, CGI proposes constructions that violate fundamental rules of claim construction, are inconsistent with the intrinsic record, and obscure the meaning of the claim.

CGI ignores the plain language of claim 1, instead proposing that limitations from the specification be imported into the claim. For

example, CGI proposes that the Court construe "in the same target double stranded polynucleotide" to require that the two strands of the polynucleotide be "linked to the solid support at or near their 5' ends." But claim 1 does not include a "solid support," nor does it require linking the strands "at or near their 5' ends." CGI also asks the Court to construe "reading from a [first/second] primer" to be limited to a particular method of "reading" sequence information. But claim 1 includes no such limitation and the specification discloses alternative methods for "reading" sequence information.

In both cases, CGI violates the rule against limiting claims to preferred embodiments described in the specification. Even where the specification discloses only a single embodiment, features of that embodiment may not be read into the claims unless the specification makes a clear disclaimer of claim scope. Here, the specification contains no such disclaimer, and expressly says the claimed pairwise method is ***not*** limited to a particular method for reading DNA sequence information, as CGI contends. CGI's constructions also violate the rule of claim differentiation by importing limitations from dependent claims into claim 1.

Moreover, CGI's proposed constructions will not aid the jury in deciding this case because they are needlessly complex and ambiguous, and will therefore confuse the meaning of the claim.

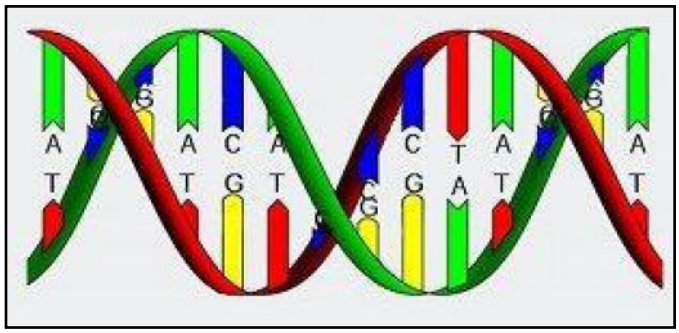
II. Factual background

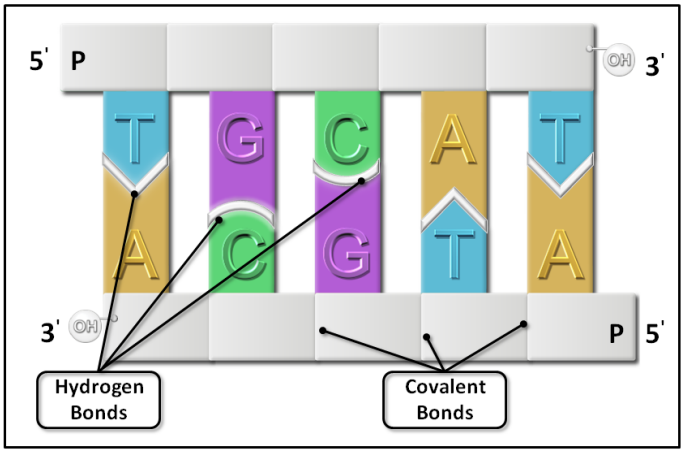
A. Structure and function of DNA

All living things contain DNA, in the form of very long strands made up of its four building blocks, called "nucleotides." The four nucleotides are referred to as A, C, G, and T. An organism's DNA sequence—that is,

the order of its A's, C's, G's, and T's—determines what proteins are made in its cells and tissues. In this way, an organism's DNA sequence determines its identity.

Each nucleotide in a strand of DNA is composed of a base, a sugar, and a phosphate group. Under the right conditions, the phosphate group of one nucleotide can covalently bond with the sugar of another nucleotide, creating a "polynucleotide" chain. The four bases of DNA (adenine (A), cytosine (C), guanine (G), and thymine (T)) are attached to the sugar-phosphate backbone of a polynucleotide chain. The bases in one strand of DNA can hydrogen-bond (or "hybridize") with the bases in another strand of DNA to form a double-stranded polynucleotide (the famous "double helix"). Such binding is "complementary": A's in one strand will only hybridize with T's in the other strand, and C's will only hybridize with G's, as illustrated at right.





A polynucleotide chain is said to be "directional" because the two ends of the chain are chemically different. One end is called the 5' (pronounced "five prime") end and the other end is called the 3' end. The phosphate group (P) is at the 5' end of the nucleotide, and it can form a covalent bond with a "hydroxyl" (OH) group at the 3' position of the sugar of another nucleotide.

B. DNA sequencing

This case involves DNA sequencing. DNA sequencing is the process of determining information about the sequence of nucleotides in a sample of DNA. Illumina manufactures, sells, and uses DNA-sequencing technologies that enable scientists to sequence DNA samples at high speeds and low costs. Using an Illumina instrument, a scientist can, for example, sequence an individual's complete DNA (a "genome")—which contains about 3 billion nucleotide pairs—in just over a day for less than $10,000. To put that in perspective, the Human Genome Project, which started in the 1990s using previous-generation technology, took thirteen years and cost almost $3 billion to sequence a single human genome. Illumina's DNA sequencing advances are revolutionizing research and paving the way for personalized medicine, in which physicians select medicines or tailor treatments specifically for each patient based on his or her DNA sequences.

C. The inventions described and claimed in the '930 patent

The inventions described and claimed in the '930 patent are methods of "pairwise" or "paired-end" sequencing. To prepare genomic DNA to be sequenced, one must first cut lengthy DNA strands into many smaller fragments. The sequence information obtained from each of these smaller fragments is then assembled by computer to create the entire genome sequence. The "pairwise" or "paired-end" methods described in the '930 patent increase the sequence information obtained from each fragment, which simplifies assembling the entire genome sequence. As the '930 patent explains:

> Paired-end sequencing allows the determination of two "reads" of sequence from two places on a single polynucleotide duplex. The advantage of the paired-end approach is that there is significantly

> more information to be gained from sequencing two stretches each of "n" bases from a single template than from sequencing "n" bases from each of two independent templates in a random fashion. With the use of appropriate software tools for the assembly of sequence information . . . it is possible to make use of the knowledge that the "paired-end" sequences are not completely random, but are known to occur on a single duplex, and are therefore linked or paired in the genome.

(Exh. A at 2:5–18.)

Claim 1 of the '930 patent states:

> A method for pairwise sequencing of first and second regions of a double stranded polynucleotide wherein said first and second regions are in the same target double stranded polynucleotide,
>
> the method comprising
>
> hybridising and reading from a first primer,
>
> removing the first primer
>
> followed by hybridising and reading from a second primer at a different location in the same target double stranded polynucleotide.

(Exh. A at 37:37–43.)

Importantly, although claim 1 is limited to these steps ((i) "hybridizing and reading from a first primer," (ii) "removing the first primer," (iii) "followed by hybridizing and reading from a second primer . . ."), it is ***not*** limited to a particular method of "reading" sequence information from a polynucleotide. Instead, the specification expressly states that the claimed methods "can be used in conjunction with ***essentially any*** sequencing methodology which relies on successive incorporation of nucleotides into a polynucleotide chain." (Exh. A at 22:9–13 (emphasis added).) The specification describes "sequencing-by-

synthesis" and "sequencing by ligation-based methods" as two of the sequencing methodologies that are compatible with the claimed methods. (Exh. A at 21:32–33 and 22:16.)

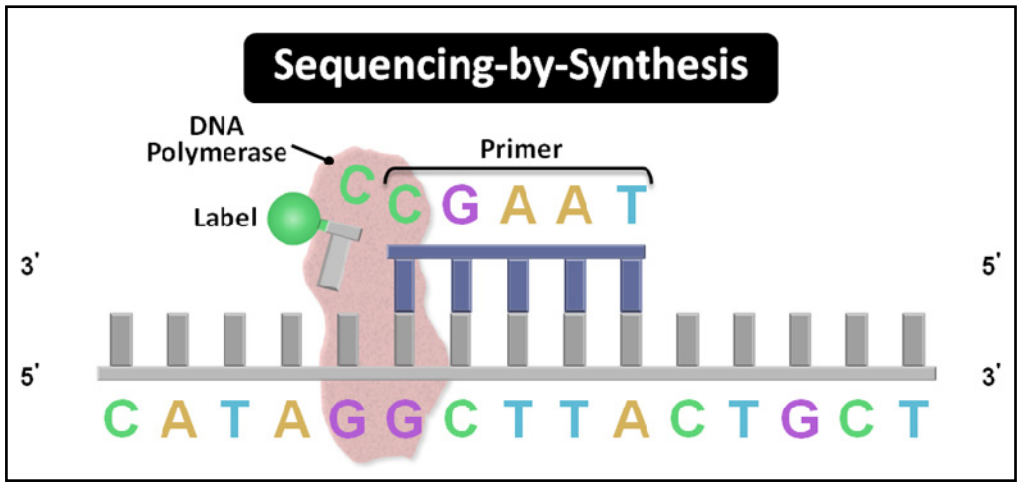
D. Methods of "reading" sequence information

Although claim 1 of the '930 patent is not limited to any particular method of reading sequence information, some background on "sequencing-by-synthesis" and "sequencing-by-ligation" methods will help place the parties' competing claim-construction arguments in context. (Exh. C at 527–530 (comparing methods of sequencing).)

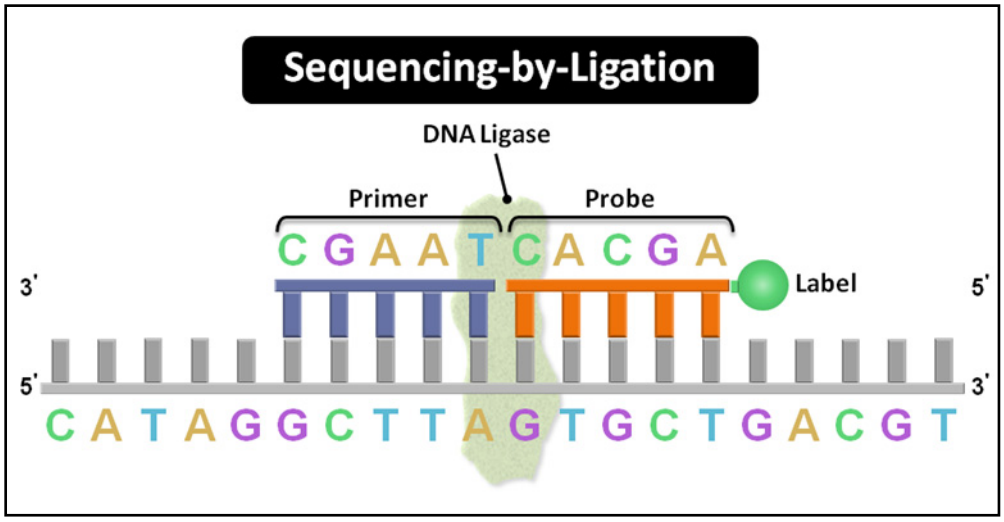
Using either "sequencing-by-synthesis" or "sequencing-by-ligation," a scientist can read sequence information from a single-stranded polynucleotide. Both methods include first hybridizing a short single-stranded piece of DNA (called a "primer") to a region of the polynucleotide near where sequencing information is desired.

After hybridizing a primer, sequencing-by-synthesis and sequencing-by-ligation employ different techniques for "reading" bases near the primer. Sequencing-by-synthesis employs the enzyme "DNA polymerase" to add a single, labeled nucleotide to the end of the primer. This enzyme catalyzes covalent bonding between the 5' end of the labeled nucleotide and the 3' end of the primer (*i.e.*, adding a nucleotide in the 5' to 3' direction). This creates an extended double-stranded "duplex" comprising the primer and one labeled nucleotide both hybridized to the polynucleotide. The label on the nucleotide identifies which nucleotide (A, C, G, or T) has been incorporated. For example, the incorporated nucleotide may have a fluorescent label attached so that if it is an "A," it will glow red when scanned with a laser, or green if it is a "C," and so on. The identity of the incorporated nucleotide can later be used to determine

the identity of the complementary nucleotide in the polynucleotide at the corresponding position (for example, if the incorporated nucleotide is an "A," the nucleotide at the corresponding position in the polynucleotide must be a "T"). This process may be repeated to obtain further sequence information near the primer.



Sequencing-by-ligation employs a different enzyme, DNA ligase, to add labeled oligonucleotide probes (short single-stranded DNA chains) to the end of a primer. DNA ligase catalyzes covalent bonding of a probe to either the 3' or 5' end of the primer (unlike in sequencing-by-synthesis, where DNA polymerase can only join a labeled nucleotide to the 3' end of the primer). This creates an extended double-stranded "duplex" comprising the linked primer and probe both hybridized to the polynucleotide. Similar to sequencing-by-synthesis, the probes used in sequencing-by-ligation can be labeled and "read" to identify one or more nucleotides within the probe. The identity of a nucleotide in the probe can later be used to determine the identity of the complementary nucleotide in the polynucleotide at the corresponding position. This process may also be repeated to obtain further sequence information near the primer.



Sequencing-by-synthesis	Sequencing-by-ligation
Uses the enzyme DNA polymerase	Uses the enzyme DNA ligase
Relies on incorporation of a single nucleotide to read sequence information	Relies on incorporation of an oligonucleotide probe to read sequence information
Nucleotides must be incorporated in the 5' to 3' direction	Probes can be incorporated in either the 5' to 3' direction or 3' to 5' direction

III. Legal standards for claim construction

The words in a patent claim "are generally given their ordinary and customary meaning." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). "[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." *Id.* at 1313. To determine the ordinary and customary meaning of the terms, the Court "should look first to the intrinsic evidence of record, *i.e.*, the patent itself, including the claims, the specification and, if in evidence, the prosecution history. Such intrinsic

evidence is the most significant source of the legally operative meaning of disputed claim language." *Vitronics*, 90 F.3d at 1582.

"[T]he claims themselves provide substantial guidance as to the meaning of particular claim terms," and "[o]ther claims of the patent in question, both asserted and unasserted, can also be valuable sources of enlightenment as to the meaning of a claim term." *Phillips*, 415 F.3d at 1314. "[T]he specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Vitronics*, 90 F.3d at 1582. However, even "if a patent describes only a single embodiment," the Court should not import limitations from the preferred embodiment in the specification if those limitations are not in the claim. *Phillips*, 415 F.3d at 1323. Finally, "[l]ike the specification, the prosecution history provides evidence of how the PTO and the inventor understood the patent." *Id.* at 1317.

"In most situations, an analysis of the intrinsic evidence alone will resolve any ambiguity in a disputed claim term. In such circumstances, it is improper to rely on extrinsic evidence." *Vitronics*, 90 F.3d at 1582.

IV. Argument

Illumina and CGI disagree on the construction of five terms in claim 1. For each term, Illumina proposes a construction that comports with the plain language of the claim and the specification (or contends no construction is necessary), while CGI attempts to create non-infringement arguments by reading unwarranted limitations into the claim terms. Most notably, although claim 1 is not limited to a particular method of reading sequence information, CGI attempts to limit the claim to sequencing-by-synthesis methods because CGI uses sequencing-by-ligation.

For convenience, here again is Claim 1, with the disputed terms in boldface:

> A method for pairwise sequencing of **first and second regions** of a double stranded polynucleotide
>
> wherein said first and second regions are **in the same target double stranded polynucleotide**,
>
> the method comprising
>
> hybridising and **reading from a first primer**,
>
> **removing the first primer**
>
> followed by hybridising and reading from a second primer **at a different location** in the same target double stranded polynucleotide.

(Exh. A at 37:37–43.)

We will address the parties' competing proposed constructions for these terms in the order they appear in Claim 1.

A. "first and second regions"

Claim Term	Illumina's Construction	CGI's Construction
"first and second regions"	"two distinct and separate single-stranded portions"	"two distinct portions of the target double-stranded polynucleotide for sequence determination. The first and second regions for sequence determination are either on the same strand, or on complementary strands, of the double-stranded polynucleotide template."

1. Illumina's construction is based on the plain language of the claim and specification

Consistent with the teaching of the specification, Illumina proposes that the Court construe "first and second regions" to mean, simply, "two

distinct and separate single-stranded portions." The specification refers to the two regions to be sequenced as "distinct and separate" regions of the polynucleotide. (Exh. A at Abstract, 1:22.) Other parts of the specification refer to "two distinct regions." (*Id.* at 3:25, 4:22.) Thus, the language "distinct and separate" expressly appears in the specification and makes clear to the jury that the two regions do not overlap.

As the specification explains, the two regions to be sequenced must be single-stranded.: "To enable two separate sequencing reactions it is in turn necessary to sequentially hybridise to two different *single-stranded* regions to serve as templates for sequencing." (Exh. A at 8:51–54; *see also id.* at 4:21–24; 13:31–33 (again referring to the "two distinct regions" to be sequenced as "single stranded").)

Figure 1 of the '930 patent illustrates that the first and second regions to be sequenced are separate and distinct. (*Id.* Fig. 1.) As illustrated in Figure 1 and explained in the specification, a first primer is hybridized to a first single-stranded region before a second primer is hybridized to a second, separate and distinct single-stranded region. (*Id.* Fig. 1 & 4:28–37.)

2. CGI's construction is unjustifiably complex

CGI agrees with Illumina that the first and second regions must be distinct and single-stranded. Specifically, CGI's construction acknowledges that the two regions are "two distinct portions of the target double-stranded polynucleotide for sequence determination." And CGI agrees that the two regions must be single-stranded because according to CGI, the two regions "are either on the same strand, or on complementary strands" of the template. But CGI's proposed construction requires additional limitations that are not in the claim

language. These additional limitations are not justifiable and obscure the meaning of the term.

First, by arguing that the two regions must be "on the same strand, or on complementary strands," CGI acknowledges that the two regions are single-stranded. But this additional limitation should not be part of the construction of ***this*** term, because the ***next*** term in the claim, "in the same target double stranded polynucleotide," already specifies the location of the two regions. The parties separately propose different constructions for that term.

Second, CGI asks this Court to construe "first and second regions" to include additional limitations beyond the plain meaning of the phrase. CGI's proposed construction uses the term "double-stranded polynucleotide *template*," which does not appear anywhere in the claim. Adding this limitation without any antecedent basis does nothing to clarify the meaning of the claim and would likely confuse the jury. Rather than introduce additional limitations not found in the claim, the Court should adopt Illumina's straightforward construction of "first and second regions" to mean "two distinct and separate single-stranded portions."

B. "in the same target double stranded polynucleotide"

Claim Term	Illumina's Construction	CGI's Construction
"in the same target double stranded polynucleotide"	"in the same strand or complementary strands derived from the original polynucleotide duplex from which sequencing information is desired"	"in the template polynucleotide duplex formed from complementary first and second template strands which are linked to the solid support at or near their 5' ends"

1. Illumina's construction is based on the plain language of the claim and specification

Illumina defines "in the same target double stranded polynucleotide" to mean that the two regions to be sequenced are in the same strand or complementary strands derived from the original polynucleotide duplex from which sequencing information is desired. Without this clarification, the jury might incorrectly assume that the two regions to be sequenced are themselves double-stranded. According to the '930 specification, "two different *single-stranded regions* . . . serve as templates for sequencing." (Exh. A at 8:53–54 (emphasis added).) The specification further explains that "[f]ormation of suitable *single-stranded regions* for sequencing can be achieved by any of the ways described herein." (*Id.* at 8:54–56 (emphasis added).) Thus, one of ordinary skill would understand that the two regions of the double-stranded polynucleotide from which sequence information is obtained are single-stranded.

Accordingly, "in the same target double stranded polynucleotide" does not mean the two regions themselves are double-stranded, but rather that they are single-stranded regions *derived from* the same double-stranded polynucleotide. Given that the two regions must themselves be single-stranded, if they were not *derived from* the *same* double-stranded polynucleotide, the claim term "in the *same* target double stranded polynucleotide" would be meaningless.

Numerous examples in the '930 specification support Illumina's construction. Figure 1, for instance, illustrates that the two regions to be sequenced are single-stranded. (Exh. A Fig. 1.) The specification explains that the "target double stranded polynucleotide" is denatured before sequencing to provide "single-stranded polynucleotides" to be sequenced. (*Id.* at 4:3–6, 9–14, 15–18, 21–24.) Figure 8 illustrates a double-stranded

polynucleotide that can be cut in two with a restriction enzyme, allowing one to take "two reads derived from the original polynucleotide duplex." (*Id.* Fig. 8 & 9:26–50.) Moreover, numerous examples in the '930 specification describe amplification (making many copies) of the original template polynucleotide for sequencing, meaning that the actual molecules that are sequenced are derived from an original polynucleotide rather than just the original polynucleotide itself. (*Id.* Figs. 4–7, 6:66–7:2.)

The specification explains (and CGI agrees) that the two "regions" to be sequenced are in the same strand, or in complementary strands, of the polynucleotide. (Exh. A at 5:54–57.) And the specification further describes the "target double-stranded polynucleotide" as "any polynucleotide that it is desired to sequence." (Exh. A at 22:18–20.) The Court should therefore construe the term to mean "in the same strand or complementary strands derived from the original polynucleotide duplex from which sequencing information is desired."

2. CGI attempts to improperly narrow the claim with additional limitations

CGI's proposed construction adds additional limitations not found in claim 1. CGI acknowledges that the double-stranded polynucleotide is a duplex with complementary first and second strands. But CGI proposes a construction that requires those strands to be "linked to the solid support at or near their 5' ends." This limitation does not appear in the claim.

Claim 1 itself shows that CGI's construction is incorrect: claim 1 says nothing about the polynucleotide strands being attached to a solid support, much less at their 5' ends. These words appear nowhere in the claim. "Quite apart from the written description and the prosecution history, the claims themselves provide substantial guidance as to the meaning of particular claim terms." *Phillips*, 415 F.3d at 1314. The Court

should not read limitations into the claim that do not appear in the claim. *Kara Tech. Inc. v. Stamps.com Inc.*, 582 F.3d 1341, 1347 (Fed. Cir. 2009) ("Here, when the inventor wanted to restrict the claims to require the use of a key, he did so explicitly. None of the claims at issue on appeal recite the term "key.").

a. CGI's construction improperly limits the claim to preferred embodiments in the specification

The Court may not limit claims to a preferred embodiment in the specification if the claims are broader than the embodiment. *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1326 (Fed. Cir. 2002) ("[L]imitations from the specification are not to be read into the claims."). "The claims, not specification embodiments, define the scope of patent protection." *Kara Tech.*, 582 F.3d at 1348. Indeed, even if the specification describes only a single embodiment, the claims should not be limited to that embodiment "unless the patentee . . . characterize[d] the invention in the intrinsic record using words or expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope." *Teleflex*, 299 F.3d at 1327; *see also Saunders Group, Inc. v. Comfortrac, Inc.*, 492 F.3d 1326, 1332 (Fed. Cir. 2007) ("Even where a patent describes only a single embodiment, claims will not be read restrictively unless the patentee has demonstrated a clear intention to limit claim scope.").

Here, CGI asks this Court find that claim 1 requires attaching the polynucleotide to a solid support, and that it must be attached at its 5' end. Neither limitation appears in the claim. CGI's improper construction is like that in *Enzo Biochem, Inc. v. Applera Corp.*, 599 F.3d 1325, 1333 (Fed. Cir. 2010), where the Federal Circuit reversed a district court's claim construction that "read a 'hybridization' requirement into the

claims." The Federal Circuit found that "[n]othing in the claims refers to hybridization, and neither the specification nor the prosecution history contains a clear disclaimer or a contrary definition." *Id.*; *see also Northrop Grumman Corp. v. Intel Corp.*, 325 F.3d 1346, 1355 (Fed. Cir. 2003). ("Absent a clear disclaimer of particular subject matter, the fact that the inventor may have anticipated that the invention would be used in a particular way does not mean that the scope of the patent is limited to that context.")

Here, the specification of the '930 patent (i) explains that the "starting point for the method of the invention is the provision of a plurality of template polynucleotide duplexes immobilized on a solid support" and (ii) describes the duplexes as "formed from complementary first and second template strands which are linked to the solid support at or near to their 5' ends." (Exh. A at 5:59–6:2.) But the concept of immobilization does not appear in claim 1. The fact that the '930 patent inventors anticipated that their invention could be used with immobilized polynucleotides attached at their 5' ends does not limit the scope of claim 1 to that embodiment absent a "clear disclaimer." *Northrop Grumman*, 325 F.3d at 1355.

b. The specification expressly contemplates alternatives to CGI's proposed construction

There is no "clear disclaimer" in the '930 patent. The specification explains that no particular method of immobilization (*e.g.*, covalent or non-covalent, at the 5' end or elsewhere, etc.) is required to perform the method of the invention: "In certain embodiments of the invention covalent attachment may be preferred, but generally all that is required is that the molecules (e.g. nucleic acids) remain immobilized or attached to the support under the conditions in which it is intended to use the

support, for example in applications requiring nucleic acid amplification and/or sequencing." (Exh. A at 6:19–25.)

According to the specification, the terms "immobilized" and "attached" are "intended to encompass direct or indirect, covalent or non-covalent attachment." (Exh. A at 6:16–18.) The specification does not assert that attaching the polynucleotide at its 5' end is the only way to practice the invention, so the claim is not so limited. *Saunders Group*, 492 F.3d at 1332 ("While an assertion by the patentee that using pressure activated seals is the only way to maintain the needed traction force would evidence an intention to narrow the scope of the independent claims, the patent contains no such assertion.").

Moreover, according to the specification, "[t]he methods of the invention are not limited to use of the sequencing method outlined [in the preferred embodiment]." The specification expressly states that the methods can be used with other techniques, including, for example, "sequencing by ligation-based methods" such as the method described in U.S. Patent No. 6,306,597 ("the '597 patent"). (Exh. A at 22:9–17.) The claims of the '597 patent do not require the polynucleotide to be attached to any solid support. (Exh. B at 21:26–34.) To the extent the written description of the '597 patent suggests the polynucleotide be attached to a solid support, it does not require any particular method of attachment. The '597 patent expressly discloses attaching the polynucleotide at either its 3' or 5' end. (Exh. B at 9:12–13, 10:35–36.)

c. CGI's proposed construction violates the rule of claim differentiation

The rule of claim differentiation weighs against reading immobilization or attachment to a solid support into claim 1. Claim 1 is the only independent claim in the '930 patent. All of the remaining

claims ultimately depend from claim 1, and all of the dependent claims include immobilization of the polynucleotide or attachment to a solid support as an additional claim limitation. (Exh. A at 37:36–40:32.) "[T]he presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Phillips*, 415 F.3d at 1315. Thus, claim 1 should not be construed to include a limitation to immobilization or attachment.

d. The prosecution history supports Illumina's construction

The prosecution history of the '930 patent also weighs against CGI's proposed construction. "Like the specification, the prosecution history provides evidence of how the PTO and the inventor understood the patent." *Phillips*, 415 F.3d at 1317. During prosecution, the patent examiner interpreted claim 1 to ***not*** require immobilization or attachment, while the examiner interpreted the remaining claims to require attachment to a surface. The examiner initially rejected claim 1 (then-application claim 27) as anticipated by (*i.e.*, all the elements of claim 1 were disclosed in) the "Weimann" reference, which she said "does not teach attachment to a clustered array" or immobilization of the polynucleotide on a solid support. (Exh. D, March 4, 2011 Office Action at 9.) But the examiner only found the remaining claims obvious based on the combination of Weimann *and* the "O'Meara" reference, which added the disclosure of "providing a solid support" with immobilized templates. (*Id.* at 5–7.) If the examiner thought claim 1 was limited to immobilization or attachment to a surface, she could not have found the claim anticipated by Weimann because she acknowledged that the attachment element was missing in Weimann. Instead, she would have also cited O'Meara as part of her rejection of claim 1.

Most notably, Illumina never disputed that claim 1 (application

claim 27) does not require immobilization or attachment, but rather amended the claim to recite "followed by" to overcome the anticipation rejection. (Exh. E, Dec. 7, 2011 Amendment & Response at 6–7; Exh. F, Apr. 2, 2012 Notice of Allowance at 2–3.) Accordingly, the prosecution history also establishes that the inventors understood claim 1 not to require immobilization or attachment.

For exactly this reason, this Court has previously refused to read an additional limitation into a claim. *Morvil Technology, LLC v. Medtronic Ablation Frontiers, LLC*, 2012 WL 3277272, at *5 (S.D. Cal. Aug. 10, 2012) (Benitez, J.). In *Morvil*, this Court rejected the defendants' proposal to incorporate a limitation into the claim where, during patent prosecution, (i) the examiner had initially found the claim anticipated by a prior art reference that lacked the same limitation the defendants sought to read into the claim and (ii) the inventors never disputed the anticipation rejection based on the missing limitation in the prior art. *Id.*

The Court should reject CGI's proposed construction because it requires that the polynucleotide be attached to a solid support, a limitation not found in the claim, let alone attachment at the 5' end.

C. "reading from a [first/second] primer"

Claim Term	Illumina's Construction	CGI's Construction
"reading from a first primer" "reading from a second primer"	"obtaining sequence information near where the [first/second] primer has hybridized"	"the successive incorporation of nucleotides into a polynucleotide chain synthesized in the 5' to 3' direction from the [first/second] primer and the determination of the nature of the nucleotide after each incorporation"

1. Illumina's construction is based on the plain language of the claim and specification

Illumina proposes that "reading from a primer" be construed to mean "obtaining sequence information near where the primer has hybridized." Illumina's construction defines "reading" to mean obtaining sequence information, and that "from a primer" means near the primer. This construction is consistent with the plain meaning of the term when read in light of the specification. First, the specification explains that "[u]sing the method of the invention it is possible to obtain two linked or paired *reads of sequence information*" from the polynucleotide template. (Exh. A at 3:27–31 (emphasis added).) The "reads of sequence information" are the result of the "reading" step in claim 1. The term "reading" in claim 1 therefore means obtaining sequence information. But, contrary to CGI's argument, obtaining sequence information, or "reading," does not require "determination of the nature of the nucleotide after each incorporation," a step which the specification refers to as a "particular embodiment." (Exh. A at 21:36–38.)

According to the '930 patent, the bases to be read "do not, however, need to be contiguous, nor does every base on the entire fragment have to be sequenced." (Exh. A at 6:46–48.) Thus, "reading from a primer" means sequence information must be obtained near the primer. It does not require determining the identity of the base immediately contiguous to the primer, or every base adjacent to the primer.

2. CGI's construction improperly excludes alternative methods of "reading" recited in the specification

CGI's claim construction is simply another attempt to limit the claim to a specific method of sequencing: sequencing-by-synthesis in the 5' to 3' direction. Although the '930 specification says that "[s]equencing can be

carried out using any suitable 'sequencing-by-synthesis' technique . . . resulting in synthesis of a polynucleotide chain in the 5' to 3' direction," (Exh. A at 21:32–36), the specification says the "methods of the invention ***are not limited to*** use of the sequencing method outlined above" (*id.* at 22:9–10 (emphasis added)). Instead, the methods of the invention "can be used with essentially any sequencing methodology which relies on successive incorporation of nucleotides into a polynucleotide chain." (*Id.* at 22:10–13.) "Suitable techniques include, for example, Pyrosequencing™, FISSEQ . . ., MPSS . . . and ***sequencing by ligation***-based methods, for example as described in U.S. Pat. No. 6,306,597." (*Id.* at 22:13–17 (emphasis added).)

The "sequencing-by-ligation-based method" described in the '597 patent is a "method of identifying nucleotides in a template by stepwise extension of one or more primers by successive ligations of oligonucleotide blocks." (Exh. B at 1:12–14.) According to the '597 patent, the extension of primers by ligation may occur in the 5' to 3' direction or the 3' to 5' direction. (Exh. B at 6:13–15, figs. 2 & 3A.) CGI's construction of "reading" to limit it to sequencing-by-synthesis in the 5' to 3' direction would exclude this method. Thus, it cannot be correct because the '930 patent recites multiples examples of how the claimed method can be used, and expressly states it is not limited to sequencing-by-synthesis.

Accordingly, CGI's proposed construction of "reading" also violates the rule against limiting claims to a preferred embodiment. Again, where the claim does not contain a particular limitation, and the specification does not contain a "clear disclaimer," the Court should not read limitations from the preferred embodiment into the claim. *Enzo Biochem*, 599 F.3d at 1333. Here, the specification lacks a "clear disclaimer" and

expressly recites alternative methods of reading that CGI's proposed construction would exclude.

D. "removing the first primer"

Claim Term	Illumina's Construction	CGI's Construction
"removing the first primer"	This term need not be construed, or if construed, the Court should construe this term as having its plain and ordinary meaning.	"heating or chemically denaturing from the surface the first sequencing primer when the first sequencing reaction is complete."

1. The Court need not construe "removing the first primer"

"Removing the first primer" does not need construction because "removing" is a commonly-understood word with no special meaning in the patent or the field of sequencing. The Court need not construe claim terms that do not require clarification. "The *Markman* decisions do not hold that the trial judge must repeat or restate every claim term in order to comply with the ruling that claim construction is for the court." *U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997). Instead, claim construction serves "to clarify and when necessary to explain what the patentee covered by the claims." *Id.* For example, "commonly-understood English words" do not need clarification. *Netflix, Inc. v. Blockbuster, Inc.*, 477 F. Supp. 2d 1063, 1068 (N.D. Cal. 2007); *see also Gen-Probe Inc. v. Becton Dickinson & Co.*, 2011 WL 7167137, at *17 (S.D. Cal. Nov. 22, 2011) (Benitez, J.) ("[T]erms 'penetrated by,' 'penetrated,' and 'penetrating' are common terms that need no clarification.").

2. CGI's construction is ambiguous and unjustifiably narrows a simple term

CGI's proposed construction adds limitations, such as "heating or chemically denaturing," that do not appear in the claim. Although

Illumina agrees that "removing" can include "heating or chemically denaturing," CGI's construction adds ambiguity and unjustifiably attempts to narrow the scope of the claim. CGI replaces a word the jury will understand—"removing"—and replaces it with a word likely unfamiliar to the jury—"denaturing." Further, the phrases "from the surface" and "first sequencing reaction" lack any basis in the claim and merely add ambiguity to an otherwise unambiguous term.

CGI also attempts to add a temporal limitation to the claim. Illumina agrees that in the context of the entire claim, the step of "removing the first primer" follows the step of "hybridizing and reading from a first primer." But the term "removing the first primer" by itself does not incorporate that requirement. CGI attempts to read the concept of a "first sequencing reaction" into the claim and require that the "first sequencing reaction" "be complete" before the first primer is removed. This is unwarranted. Although claim 2 refers to a "first sequencing reaction," (Exh. A at 37:57), that limitation does not appear in claim 1. Therefore, adding the requirement that the "first sequencing reaction be complete" before removing the first primer violates the rule of claim differentiation and would only add confusion, not clarity to the claim.

Finally, CGI once again attempts to incorporate a "surface" limitation into claim 1, although that limitation does not appear in the claim. (*Supra* section IV.B.2.)

The Court should not construe "removing the first primer" because the term does not require clarification and CGI's proposed construction is ambiguous and unduly narrow.

E. "different location"

Claim Term	Illumina's Construction	CGI's Construction
"different location"	"a location distinct and separate from the location of hybridizing and reading from the first primer"	"location of the second region that is distinct from the first region"

1. Illumina's construction makes clear what occurs at a "different location"

Claim 1 requires "hybridizing and reading from a first primer . . . followed by hybridizing and reading from a second primer at a different location." Illumina offers a construction of "different location" to make clear that "different location" modifies "hybridizing and reading from a second primer." This is to say that the "different location" is distinct and separate from the hybridizing *and* reading from the first primer.

Illumina's construction is dictated by the plain language of claim 1. The term "at a different location" immediately follows and modifies the phrase "hybridizing and reading from a second primer." And the term distinguishes the location of the "hybridizing and reading from the second primer" from the previously-recited "hybridising and reading from the first primer." Thus, a contextual reading of claim 1 supports Illumina's proposed construction.

In contrast, CGI replaces the actual claim language with the phrases "second region" and "first region." CGI defines "different location" to mean that the *second* region is different from the *first* region, which provides no clarification: the jury must study the claim to decide what qualifies as the "first region" and what qualifies as the "second region." Illumina's construction is better because it explicitly tells the jury that *both* hybridizing *and* reading must occur at distinct and separate

locations. Illumina's construction makes clear *what* must occur at a "different location," and properly defines the term "different location" in the context of what the claim actually says.

Illumina's construction is also consistent with the specification. The specification explains that both hybridizing and reading occur at different locations. Regarding hybridizing, the '930 specification explains that "it is in turn necessary to sequentially hybridize to two *different single-stranded regions* to serve as templates for sequencing." (Exh. A at 8:52–54 (emphasis added).) And with respect to reading, the specification explains that "pairwise sequencing refers to *a pair of reads* obtained by sequencing *two distinct regions*." (Exh. A at 3:23–25 (emphasis added).)

Finally, the '930 specification states the two different regions are "distinct and separate." (Exh. A at Abstract, 1:19–23.) The term "different location" therefore requires distinct and separate locations for both hybridizing and reading.

V. Conclusion

For all of the foregoing reasons, the Court should adopt Illumina's proposed claim constructions and reject CGI's proposed constructions.

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Respectfully submitted,
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